UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/199,340	04/03/98	LLORIN	

EXAMINER	
WARE, D	F 4270

ART UNIT	PAPER NUMBER
1651	

HM22/1215

RICHARD RODRICK
BECTON DICKINSON & COMPANY
1 BECTON DRIVE
MAIL CODE 089
FRANKLIN LAKES NJ 07417-1880

DATE MAILED: 12/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Patent and Trad[illegible]k Office
ASSISTANT SECRETARY AND COMMISSIONER OF
PATENTS AND TRADEMARKS
Washington, D.C. 20231

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20

Application Number: 09/128,340
Filing Date: August 3, 1998
Appellant(s): Llorin et al.

David W. Highet
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed June 29, 2000.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct, however, the rejection of claims 5-13 under 35 USC 112, second paragraph, is now removed; and the only rejection remaining is the issue regarding 35 U.S.C. 103(a) for all pending claims (1 and 3-13).

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1 and 3-13 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

Buck, G.E. "Rapid, Simple Method for Treating Clinical Specimens Containing *Mycobacterium tuberculosis* To Remove DNA for Polymerase Chain Reaction." Journal of Clincal Microbiology, vol. 30, no. 5 (May 1992), pp. 1331-1334.

U.S. Pat. No. 3,887,431	Robbins et al.	June 3, 1975
U.S. Pat. No. 5,376,527	Robson et al.	Dec. 27, 1994

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

I. Claims 1 and 3-13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Buck et al. (PTO-1449 Form, Paper No. 5) in view of Robson et al. (PTO-1449 Form, Paper No. 3) and Robbins et al. (PTO-892 Form, Reference A).

Claims 1 and 3-13 are drawn to a method for disrupting cells using ultrasonic energy without beads wherein the cells are in a liquid at an alkaline pH. The method is applied to mycobacterial cells. Further, claim 8 is drawn to a method for disrupting cells by applying ultrasonic energy to a sample of cells in a liquid having reduced surface tension.

Buck teaches a method for disrupting *Mycobacterium tuberculosis* cells using ultrasonic energy without beads (page 1331, abstract). This is done by providing a sonic bath comprising a first liquid (i.e. dish of water next to a sonicator probe), and placing into the first liquid a vessel comprising cells in a second liquid (i.e. tubes containing the cells within another liquid, such as residual water or buffer solution or detergent solution). Furthermore, several procedures for disruption of the cells are disclosed (page 1331, second column, all lines, procedures (i) through (iv)). In addition, use of a liquid having an alkaline pH (i.e. pH 8.3) for disrupting cells is also described (page 1331, second col., (i) treatment procedure, all lines). Although surfactants are well known in the art to reduce or alleviate surface tension in liquids, this point is silent in the art. However, Buck describes Triton X-100 and Tween to be useful for cell disruption. These are well known surfactants in the art. Tris-HCl is also described by Buck to be useful for cell disruption.

Robson teaches a process for lysing Mycobacteria (i.e. *Mycobacterium tuberculosis*) cells using an effective amount of heat (col. 1, lines 40-48) and surfactant-containing liquids having an alkaline pH, note col. 4, line 40 and col. 6, lines 25-42. Note that Robson teaches that cells to be lysed can be in water, but also can be in suitable buffers having alkaline pH (i.e. Tris-HCl, pH 8.0, pH. 8.8, etc.). Also Robson teaches disrupting Mycobacteria cells using sonication, with and without glass beads, and heat at 60 °C, note cols. 8-9, all lines.

Robbins teaches a method for disrupting cells using ultrasonic energy (i.e. sonic disintegration) and adjusting the disrupted cells at an alkaline pH between 8 and 11, and a temperature of 4° C to 60 ° C (col. 3, lines 18-55).

The claimed subject matter differs from the disclosure of Buck in that an alkaline pH is not clearly taught as a requirement during sonication.

It would have been obvious to one of ordinary skill in the art at the time of Appellants' invention to combine the process disclosed by Buck with the disclosures of Robson and Robbins in order to provide for conditions of alkaline pH during sonication. One of skill would have been motivated to use an alkaline liquid containing buffers and surfactants to enhance disruption of the cells during ultrasonication with and without beads. Clearly one of skill in the art would have expected this liquid containing the cells to provide for optimal cell disruption in order to enhance recovery of releasable cell products after disintegration of the cells.

Whether the first liquid or second liquid contains the cells is only important with respect to the alkaline pH conditions and ultrasonic disruption of the cells. The modification of a requirement for alkaline pH conditions during ultrasonication is clearly obvious to one of ordinary skill in the art. In addition, the art clearly recognizes the means by which surface tension of liquids may be reduced. Surface tension is reduced by the addition of surfactants. The judicious selection of a surfactant can change the pH conditions of any liquid. This is well known to those of ordinary skill in the art.

Also since surfactants are well known in the art to reduce surface tension, the reduced surface tension of the liquid containing the cells is the result expected of a liquid containing a surfactant. Thus, the reduced surface tension of the liquid is merely an expected successful result. Because this result is obtained by an obvious modification of the prior art, the reduction in surface tension of the liquid is obvious.

Therefore, all of the elements of the claims are taught, or at least suggested, by the cited prior art. These are as follows:

1) ultrasonic energy for disrupting cells in the presence or absence of beads;

2) use of two liquids wherein one liquid contains the cells in a vessel and the other is used in a sonic bath wherein the temperature is about 60° C;

3) the cells are mycobacterial cells;

4) the liquid containing the cells is at an alkaline pH; and

5) the liquid containing the cells has a reduced surface tension.

Thus, the claims are *prima facie* obvious over the cited prior art.

(11) Response to Argument

I. Rejection under 35 U.S.C. 103

Claim 1

1. Appellants argue that the assertions regarding Buck are incorrect. However, Buck is combined with two other secondary references, Robson and Robbins, but even alone Buck teaches the various steps leading to alkalinization of a sonication solution. All three of

the described procedures used for comparison of the effectiveness of these method steps teach the alkalinization of a sonication solution. Treatment procedure (i) clearly describes a lysing solution containing PCR buffer (10 mM Tris-HCl [pH 8.3], 50 mM KCl, 1.5 mM $MgCl_2$, 0.001T gelatin) with 0.45% Tween 20 (Sigma) and 0.45% Triton X-100. Thus, the argument that methods i, ii and iii of Buck are not critical to cell disruption is not deemed persuasive

Further, Robson and Robbins clearly teach the use of alkaline solutions for disrupting cells. Also Robson specifically teaches that cell disruption may be carried out in water, as well as in buffer solutions and solutions containing surfactants. In addition Buck suggests the desire in the art to combine the described procedures to obtain an enhanced cell disruption method. Therefore, the motivation to combine Buck with Robson and Robbins becomes even more clear to one of skill in the art.

Board did not address this conclusion of my motivation analysis

2. Appellants argue that there are significant differences between the teachings of Buck and the claimed invention. However, the differences upon which Appellants rely are not sufficient to overcome Buck. A dish of water next to a sonicator probe suggests a sonic bath to one of ordinary skill in the art. Furthermore, Buck teaches sonication appears to be a simple, rapid means for disrupting cells containing *M. tuberculosis* to remove DNA for amplification (page 1333, second col., last para., all lines). Further, this bacteria is taught by Robson to be generally heat resistant (cols. 1-2, all lines). Therefore, the use of the sonic bath described by Buck would not have been expected to be problematic. Thus, Appellants' argument is unpersuasive.

what was meant here is that the bacteria are very resistant and that heat alone would not be expected to work, thus always effective amount of heat as required as the bacteria are generally well understood

3. Appellants argue the teachings of Robson fail to adequately address the significant differences between the teachings of Buck and the claimed invention. However, the deficiency of Buck is only with respect to an explicit teaching for the use of a liquid having an alkaline pH. Robson clearly remedies this deficiency since the cells to be disrupted can be in water, but also can be in suitable buffers such as PCR and detergents such as Tween and Nonidet P-40 (col. 6, lines 25-40). The cell-disrupting-solutions are clearly at an alkaline pH.

In addition, Buck and Robson both teach sonication with and without beads. Nowhere in Buck is there a mention of sonication with beads. Robson teaches sonication without beads in example 2, and sonication with beads in example 4. The combination of the cited prior art clearly suggests to perform sonication without beads. Further Appellants argument, regarding results obtained by Robson do not constitute a teaching that can be characterized as providing those of skill in the art with a reasonable expectation of success for the claimed invention, is unpersuasive. Because the sonication without beads in example 2 did release some of the DNA. The claimed invention does not require a specific amount of cellular product to be released. Nor does the claimed invention require the release of any product from the disrupted cells.

4. Appellants' argue the teachings of Robbins fail to adequately address the significant differences between the teachings of Buck and the claimed invention. Robbins teaches that the cells are ruptured by any of several known methods including sonic disintegration (col. 3, lines 20-23). Further, Robbins teaches the most important factor is to

rupture the cells under conditions such that the releasable products will not be destroyed (col. 3, lines 25-36). The disrupted cells are adjusted at an alkaline pH. However, one of skill in the art would have expected pH conditions to change from one cell type to the next. Thus, to select for appropriate pH conditions for cells is an obvious modification in a cell disruption method. Therefore, Buck combined with Robson and Robbins clearly suggests the selection of alkaline pH conditions and a temperature of about 65 ° C.

5. Appellants' conclusion that there are significant differences between the combination of cited references and the claimed invention is not well-founded because the motivation in the cited prior art to provide for alkaline conditions during ultrasonication is clear. One of ordinary skill in the art would have been led by the teachings of Buck in view of Robson and Robbins to select for conditions based on the cells being disrupted. The alkaline pH conditions are obvious because Buck suggests the desire to combine procedures for purposes of enchancing the cell disruption process. Robbins teaches the importance of such conditions during the cell disruption process. Robson clearly teaches alkaline pH conditions during ultrasonication. The motivation in the art to use alkaline pH conditions is clear from the teachings of the combined cited prior art. Use of alkaline pH conditions are an obvious modification to ultrasonication methods for purposes of disrupting cells. The claim is *prima facie* obvious for those reasons discussed above.

Claim 3

Claim 3 depends from claim 1, and thus all of the arguments above for claim 1 are equally applicable for claim 3. The use of heat as taught by Buck and Robbins clearly motivates the use of a temperature range for cell disruption. Appellants set forth the limitation of claim 3 (temperature of "about 65 °C to about 75 °C"). Although the limitation is not disclosed by Buck, this limitation is at least suggested by Robson which teaches sonication at 60°C at column 8, line 59 and column 9, line 18. Sonication at 60 °C is close to 65 °C and is deemed to be encompassed by "about 65°C". Therefore, this argument is unpersuasive.

Claim 4

Claim 4 depends from claim 3, which depends from claim 1, and thus all of the arguments above for claims 1 and 3 are equally applicable for claim 4. Appellants argument that Robbins teaches the rupture of yeast cells is noted. However, Robbins also teaches the rupture of bacteria cells since the bacteria would have been expected to be present due to contamination factors (col. 5, all lines). Thus, there is no negative teachings set forth by the disclosure of Robbins.

Mycobacteria cells are clearly disclosed by Buck and Robson. Therefore, the motivation of the cited combined prior art is clear with respect to what cells may be subjected to cell disruption.

Therefore, the art is clear that Mycobacterial cells under appropriate conditions would have been expected to be successfully disintegrated using ultrasonication. Appellants' argument is unpersuasive.

Claim 5

Claim 5 depends from claim 1, and thus all of the arguments above for claim 1 are equally applicable for claim 5. Appellants' argument that the cited prior art fails to teach reduction of surface tension of any liquid is noted. However, the surface tension of any liquid containing a surfactant and/or buffer solution would have been expected to be reduced. The cited prior art clearly discloses these types of liquids that contain surfactants. Surfactants are well known to reduce surface tension. Therefore, this argument is unpersuasive.

Claim 6

Claim 6 depends from claim 5, which depends from claim 1, and thus all of the arguments above for claims 1 and 5 are equally applicable for claim 6. Appellants' argument that Buck does not disclose the temperature is noted. However, the argument that Robson does not cure this deficiency is unpersuasive. Robson teaches a temperature of 60°C which is deemed to be encompassed by the claimed temperature range of "about 65°C to about 75°C". The use of heat as taught by Buck and Robbins clearly motivates the use of a temperature range for cell disruption. Therefore, the argument is unpersuasive.

Claim 7

Claim 7 depends from claim 6, which depends form claim 5, which depends from claim 1, and thus all of the arguments above for claims 1, 5 and 6 are equally applicable for claim 7. Appellants argument that Robbins teaches the rupture of yeast cells is noted. However, Robbins also teaches the rupture of bacteria cells since they would have been expected to be present due to contamination factors (col. 5, all lines).

Therefore, the motivation of the cited combined prior art is clear with respect to what cells may be subjected to cell disruption. Mycobacteria cells are clearly disclosed by Buck and Robson. Thus, there is no negative teachings set forth by the disclosure of Robbins. Therefore, the art is clear that Mycobacterial cells under appropriate conditions would have been expected to be successfully disintegrated using ultrasonication. Appellants' argument is unpersuasive.

Claim 8

1. Appellants argue there are significant differences between the teachings of Buck and the claimed invention. However, Buck teaches sonication of mycobacteria in a solution. This solution may contain a surfactant. A solution is expected to include a mixture of ingredients, such as surfactants. Surfactants are well known in the art to reduce the surface tension of liquids. Therefore, one of ordinary skill in the art would have expected reduced surface tension of the liquid.

Further, Buck is combined with secondary references to show that alkaline pH conditions of the liquid for sonication are important for product yield upon cell disruption. Claim 8 is drawn to a process for disrupting cells by applying ultrasonic energy to a sample of cells in a first liquid, wherein the surface tension of said first liquid is reduced. This liquid must have a surface tension, which is actively reduced in the claimed process. Buck and the secondary references teach surfactants which are recognized in the art to reduce surface tension.

Although reduced surface tension of the liquid may be silent in the cited prior art, the presence of a surfactant in a buffer to provide for the liquid at an alkaline pH would have been expected by one of ordinary skill in the art to reduce the surface tension of the liquid. This point finds factual basis in the art at large, and is an inherent property of liquids containing surfactants and buffers.

2. Appellants argue the teachings of Robson fail to adequately address the significant differences between the teachings of Buck and the claimed invention. The exemplified disclosure of Robson is not the basis of the rejection. Robson teaches cells to be lysed can be in water, but also can be in suitable buffers, such as Tris-buffered saline (pH 8.0), and in detergents, such as 0.5% Tween 20 and 0.5% Nonidet P-40 surfactants (col. 6, lines 25-40).

Further, Buck is combined with Robson to further emphasize the functionally equivalent uses of water and surfactants as lysing solutions for cell disruption methods. In

addition, the obviousness of their alternative uses for the disruption of cells is further emphasized by the cited combination of prior art.

Also, claim 8 is drawn to a process for disrupting cells by applying ultrasonic energy to a sample of cells in a first liquid, wherein the surface tension of said first liquid is reduced. This liquid must have a surface tension, which is actively reduced in the claimed process. Buck and Robson teach surfactants which are recognized in the art to reduce surface tension.

Therefore, reduced surface tension of the liquid would have been reasonably expected based on the teachings of Buck in view of Robson.

3. Appellants argue the teachings of Robbins fail to adequately address the significant differences between the teachings of Buck and the claimed invention. Buck is combined with Robson and Robbins in order to show the obviousness of disrupting cells by applying ultrasonic energy to a sample of cells in a liquid wherein the surface tension of the liquid is reduced. Robbins does teach the presence of alkali solution (col. 3, line 19-20). Robson teaches that such alkali solutions may contain surfactants. One of ordinary skill in the art would have reasonably expected the surface tension of such solutions to be reduced. In addition, the silence of the specific terminology "reduced surface tension" in the cited prior art is not sufficient to overcome the art when the result is known.

Therefore, reduced surface tension of the liquid would have been reasonably expected based on the teachings of Buck in view of Robson and Robbins.

4. Appellants' conclusion that there are significant differences between the combination of cited references and the claimed invention is not well-founded. Because the motivation and suggestion in the cited prior art to reduce the surface tension of a sonication solution to enhance cell disruption is clear, or at least clearly suggested. One of ordinary skill in the art would have been led by the teachings of Buck in view of Robson and Robbins to select for conditions based on the cells being disrupted. The reduced surface tension of the liquid is obvious because Buck suggests the desire to combine procedures for purposes of enchancing the cell disruption process. Robbins teaches the importance of such conditions during the cell disruption process. While Robson clearly teaches the use of a sonication solution containing surfactants during ultrasonication. Buck clearly suggests this too. The motivation in the art to reduce surface tension is at least clearly taught, or at least suggested, from the teachings of the combined cited prior art. To reduce the surface tension of a sonication solution is an obvious modification to a method of disrupting cells. The claim is *prima facie* obvious for those reasons discussed above.

Claim 9

Claim 9 depends from claim 8, and thus all of the arguments above for claim 8 are equally applicable to claim 9. Appellants argue that claim 9 calls for the use of a vessel in a sonic bath and that this is a significant difference between the teachings of Buck and the claimed invention. However, the differences upon which Appellants rely are not sufficient to overcome Buck.

A dish of water next to a sonicator probe suggests a sonic bath to one of ordinary skill in the art. The test tubes, disclosed by Buck, placed in the bath suffice to read on a vessel. Furthermore, Buck teaches sonication appears to be a simple, rapid means for disrupting cells containing *M. tuberculosis* to remove DNA for amplification (page 1333, second col., last para., all lines). Further, this bacteria is taught by Robson to be heat resistant (cols. 1-2, all lines). Therefore, the use of the sonic bath described by Buck would not have been expected to be problematic in a method for disrupting cells. Thus, Appellants' argument is unpersuasive.

Further, Apellants continue to argue that Robson and Robbins fail to teach a sonic bath. However, these references are not required to specifically teach a sonic bath since Buck clearly teaches, or at least suggests, a sonic bath. Furthermore, Robson and Robbins both appear to read on a sonic bath because they use heat and sonication. Thus, Appellants' argument is unpersuasive.

Also, Appellants continue their argument regarding the lack of the cited references to suggest or motivate one of skill to reduce the surface tension of a sonication solution. However, the motivation and suggestion to reduce the surface tension is clearly evident in the prior art. Because one of skill would have known that such result would have been expected by the presence of a surfactant or buffer (containing a surfactant), as disclosed by the cited prior art. Similarly, the use of beads is well known to the ordinary artisan. Further, beads are clearly disclosed by Robson (col. 8, all lines). Thus, Apellants' argument is unpersuasive.

Claim 10

Claim 10 depends from claim 8, and thus all of the arguments above for claim 8 are equally applicable to claim 10. Appellants argue that Buck and Robbins fail to teach the presence of beads in the liquid. However, Appellants concede that Robson does teach the use of beads, but does not provide a reasonable expectation of success for their use. The use of beads are well known in the sonication art. Therefore, to use the beads or not to use the beads is merely a matter of judicious choice and selection amongst those of ordinary skill in the art. Therefore, to omit the beads or include them is an obvious modification and dependent upon the choice of conditions which are taught by Robbins to be critical during the cell disruption process. Therefore, the selection of beads would have also been an obvious choice to one of ordinary skill in the art.

Buck and Robson further teach alkaline conditions. They also teach the use of surfactants in a sonication solution. To combine these teachings, alkaline sonication solutions (containing surfactants) in the absence or presence of beads, to enhance ultrasonication for disrupting cells is obvious. Appellants' argument is unpersuasive.

Regarding the Appellants' arguments about reduced surface tension, these arguments were addressed previously for claim 8 and will not be repeated.

Claim 11

Claim 11 depends from claim 8, and thus all of the arguments above for claim 8 are equally applicable to claim 11. Appellants argue the teachings of Robbins fail to

adequately address the significant differences between the teachings of Buck and the claimed invention. Appellants argue that the assertions regarding Buck are incorrect. However, Buck is combined with two secondary references (Robson and Robbins), but even alone Buck teaches the various steps leading to alkalinization of a sonication solution. Treatment procedure (i) clearly describes a lysing solution containing PCR buffer (10 mM Tris-HCl [pH 8.3], 50 mM KCl, 1.5 mM $MgCl_2$, 0.001T gelatin) with 0.45% Tween 20 (Sigma) and 0.45% Triton X-100. Thus, the argument that methods i, ii and iii of Buck are not critical to cell disruption is unpersuasive.

Further, Robson and Robbins clearly teach the use of alkaline solutions for disrupting cells. Also Robson specifically teaches that cell disruption may be carried out in water, as well as in buffer solutions and solutions containing surfactants. Therefore, this remedies the alleged argument that there is no suggestion that PCR buffer would be a suitable alternative to water.

In addition Buck suggests the desire in the art to combine the described procedures to obtain an enhanced cell disruption method. Therefore, the motivation to combine Buck with Robson and Robbins becomes even more clear to one of skill in the art.

Appellants argue the teachings of Robson fail to adequately address the significant differences between the teachings of Buck and the claimed invention. However, the deficiency of Buck is only with respect to an explicit teaching for the use of a liquid having an alkaline pH. Robson clearly remedies this deficiency since the cells to be disrupted can be in water,

but also can be in suitable buffers such as PCR and detergents such as Tween and Nonidet P-40 (col. 6, lines 25-40). The cell-disrupting-solutions are alternatively taught to be at an alkaline pH. Thus, the use of a lysing solution at an alkaline pH is taught, or at least suggested by the teachings of Buck and Robson.

In regard to Robbins, this cited disclosure was provided to show the importance of conditions during sonication. In addition, Robbins suggest an alkali solution.

Therefore, Appellants' descriptive arguments regarding Robbins' disclosure are not applicable to the motivation provided by cited combination of prior art. The reasonable expectation of success and motivation is provided by the cited prior art as applied in combination with Buck in view of Robson and Robbins. Therefore, the piece meal arguments presented by Appellants are unpersuasive.

Claim 12

Claim 12 depends from claim 9, which depends from claim 8, and thus all of the arguments above for claims 8 and 9 are equally applicable to claim 12. Although Buck does not appear to suggest or teach a temperature of about 65° C to about 75° C, Robson clearly teaches sonication at 60° C in Examples 2, 4 and 5, which is deemed to be encompassed by "about 65°C." The claimed temperature range is so close to the temperature disclosed by Robson that one of skill would have a reasonable expectation of successful results for carrying out the sonication at about 65 ° C. Therefore, Appellants' arguments are unpersuasive.

Regarding the Appellants' arguments about reduced surface tension, these arguments were addressed previously for claim 8 and will not be repeated.

Claim 13

Claim 13 depends from claim 12, which depends from claim 9, which depends from claim 8, and thus all of the arguments above for claims 8, 9 and 12 are equally applicable to claim 13. Appellants' argument concedes that Buck and Robson disclose sonication of mycobacterial cells. Robbins also teaches the rupture of bacteria cells since bacteria may be present due to contamination factors (col. 5, all lines). Therefore, the rupture of mycobacterial cells is at least suggested by Robbins when taken in combination with the teachings of Buck and Robson. Appellants' argument is unpersuasive.

Conclusion

One of ordinary skill in the art would have had a reasonable expectation of success to apply ultrasonication to mycobacterial cells given the teachings of the cited combination of prior art. The rejection was presented in a unfragmented format wherein the intention was to provide the motivation for one of skill to select for alkaline pH conditions for disrupting cells. Clearly the motivation for selecting a liquid at an alkaline pH is present in the art. One of skill would have expected successful results for disrupting mycobacterial cells contained in a liquid at an alkaline pH.

Further, one of skill would have expected successful results for ultrasonicating mycobacterial cells contained in a liquid wherein the surface tension is reduced. The latter

based on what is expected by the presence of surfactants in a sonciation solution. Although the cited prior art may be silent about a sonciation solution wherein the surface tension of the solution is reduced, it is clear that a sonication solution is useful for disrupting cells. The claims are *prima facie* obvious.

For all of the above reasons, it is believed that the rejection should be sustained.

Respectfully submitted,

Deborah K. Ware
December 12, 2000

DEBORAH K. WARE
PATENT EXAMINER

Michael G. Wityshyn
Supervisory Patent Examiner
Technology Center 1600

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

Conferee